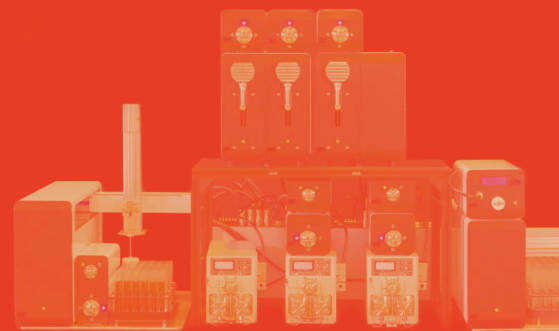# Photo Minisci reaction: 2-liquid mixture reaction

Overview

The basic 2-line system performs photoreactions in this application example. In addition to measuring and feeding optimum amounts of reagents, the **OptimFlow** enables reactions under LED lighting for photoreactions. The following illustrates an example of simplified library synthesis with the substrate and the catalyst for one reagent being premixed.
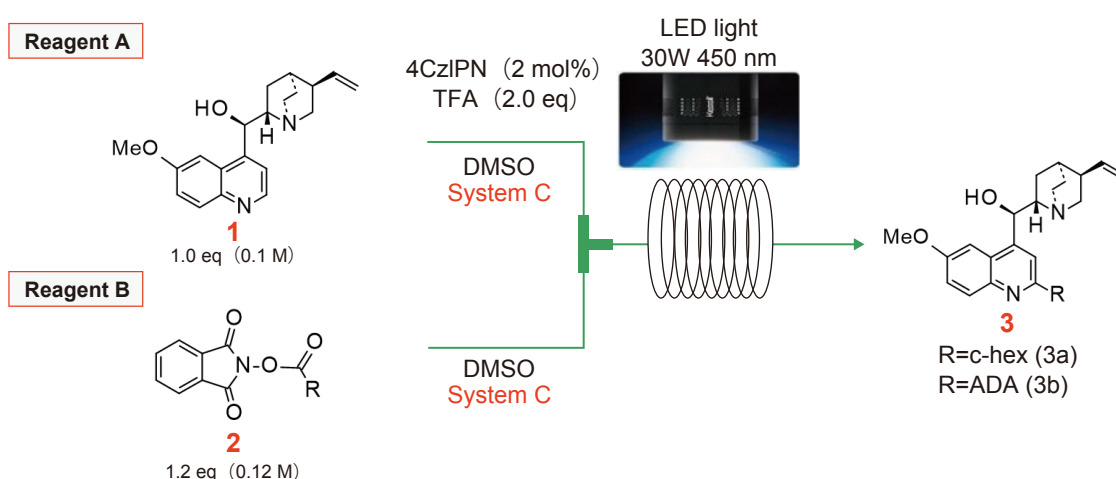
Preparation of Reagents

Reagent A: (-)-quinine 1 (64.9 mg, 0.20 mmol), 4CzIPN(2,4,5,6-tetra(9H-carbazol-9-yl)isophthalonitrile) (3.2 mg, 0.004 mmol) as a photocatalyst, and trifluoroacetic acid (30 μL, 0.40 mmol) were dissolved in DMSO (2 mL) and received nitrogen gas injection for about 3 min.

Reagent B1: (1,3-dioxoisoindolin-2-yl)cyclohexanecarboxylate 2a (65.6 mg, 0.24 mmol) was dissolved in DMSO (2 mL) and received nitrogen gas injection for about 3 min.

Reagent B2: Similarly, (1,3-dioxoindolin-2-yl)adamantane-1-carboxylate 2b (78.1 mg, 0.24 mmol) was dissolved in DMSO (2 mL) and received nitrogen gas injection for about 3 min.

Device Setup

Line 1, System C ver.3.1; Line 2, System C ver.3.1
BPR = 0.5 MPa, the 2-reagent mode with a T-shaped mixer

Reactors

A bundle of PTFE tubes (each with an inner diameter of 0.5 mm, a length of 10 m, and a capacity of 1.98 mL) was placed in a PhotoRedOx Box (HepatoChem, Inc.) and set in the **OptimFlow**. The light source used was an LED lamp (30 W, 450 nm).

Fraction Collector

In each experiment, the reaction solutions were collected together in a test tube with the Pre Stream Ratio set to 20% and the Post Stream Ratio to 30%.

Experiment

The parameters for each experiment were set as shown in the software input example (Experimental parameter).The reaction times (Residence Time) were 10, 5, and 3 min, and the reference amount of Reagent A (Volume of Reagent 1) was 300 µL. The concentration (0.10 M) of Reagent A after preparation was input into Conc. of Reagent 1 in Expts. 1 to 6. The concentration (0.12 M) of Reagent B1 was input into Conc. of Reagent 2 in Expts. 1 to 3, and the concentration (0.12 M) of Reagent B2 was input into Conc. of Reagent 2 in Expts. 4 to 6. Equivalents (1.00 and 1.20) of the reagents were respectively input into the Mol Ratio of Reagents 1 and 2.

For the Fraction collector, the Pre Stream Ratio was set to 20% and the Post Stream Ratio to 30%. To collect all reaction solutions in a test tube in each experiment, the Fraction Volume was set to 10000 µL.

The flow rates, the amounts of reagents used, and the total amount of reaction solutions in the above settings can be viewed in the Calculated value tab.

Exprimental Parameter

Calculated value

After sequential reactions at room temperature, 5 µL of each resulting reaction solution was diluted with 200 µL of DMF and analyzed with a UHPLC-MS.The conversion ratio was calculated as the ratio to the product 3a or 3b and an unreacted raw material 1 using area normalization with the ELSD area value.From (1,3-dioxoisoindolin-2-yl)cyclohexanecarboxylate 2a, (R)-(2-cyclohexyl-6-methoxy-4-quinolyl)-[(2S,4S,5R)-5-vinylquinuclidin-2-yl]methanol 3a was obtained with the yields shown in the left table below.From (1,3-dioxoisoindolin-2-yl)adamantane-1-carboxylate 2b, (R)-[2-(1-adamantyl)-6-methoxy-4-quinolyl]-[(2S,4S,5R)-5-vinylquinuclidin-2-yl]methanol 3b was obtained with the yields shown in the right table below.

R=c-hex run	RT (min)	3a (%)	1 (%)	2a (%)	conv. (%)
1	10	63	28	8	69
2	5	41	36	20	53
3	3	25	45	28	36

R=ADA run	RT (min)	3b (%)	1 (%)	2b (%)	conv. (%)
1	10	85	11	-	89
2	5	78	14	5	86
3	3	53	17	27	76